Title: "An Apparatus and method for monitoring a vascular access of a patient subjected to an extracorporeal blood treatment."

DESCRIPTION

Background of the Invention.

5   The invention relates to a system for monitoring vascular access in a patient undergoing extracorporeal blood treatment.

Specifically, though not exclusively, the invention can be usefully applied in the field of extracorporeal treatment for kidney failure.

10 Setting up an extracorporeal blood treatment, such as for example hemodialysis therapy, requires blood circulation in an extracorporeal circuit connected to the cardiovascular circuit of the patient through a vascular access.

The blood, taken from the patient and sent through an
15 extracorporeal circuit, is subjected to a treatment, generally passing through a treatment unit (for example a dialyzer filter) and thereafter returned to the patient. The vascular access is where the blood is removed from the cardio-vascular system of the patient and returned to the system.

20 One of the vascular accesses most commonly used in hemodialysis therapy is the Cimino-Brescia artero-venous fistula access. Other vascular access types are known, however. For reasons of simplicity the present description will make reference to the artero-venous fistula as an example of vascular access, without
25 excluding other types of vascular access from the claimed field of protection.

In an extracorporeal treatment the blood is usually taken from the vascular access by an arterial needle fluidly connected to the extracorporeal circuit. After having passed through the
30 treatment unit, the blood is sent back to the vascular access through a venous needle. Generally blood circulation in the

extracorporeal circuit is performed by a positive displacement pump, generally peristaltic.

One of the problems of extracorporeal blood treatment is monitoring the efficiency of the vascular access.

5 A parameter indicative of this efficiency is the blood flow rate which the vascular access can supply. This flow rate is usually greater than the blood flow rate through the extracorporeal circuit. For example, in normal conditions the blood flow rate at the vascular access is about 800÷1200 ml/minute, while the

10 blood flow rate in the extracorporeal circuit varies between 100 and 700 ml/minute.

The flow rate at the vascular access can diminish due to a vascular pathology, such as, for example, a stenosis, i.e. a narrowing of the blood passage section, or for example due to a

15 drop in cardiac output. The presence and location of a stenosis at the vascular access should be determined as soon as possible in order to prevent the stenosis degenerating into a thrombosis (occlusion of the blood vessels).

A reduced-efficiency vascular access can lead to the undesirable

20 phenomenon of recirculation of blood during treatment. Recirculation consists in the presence during treatment of blood flow proceeding in an opposite to the desired direction, i.e. from the return zone of the treated blood (venous needle) to the supply zone of the blood to be treated (arterial needle). Flow

25 recirculation therefore consists in return (in the extracorporeal circuit) of blood which has already been subjected to treatment, with a consequent diminution in treatment efficiency.

Various systems have been proposed for monitoring vascular

30 access and, more generally, the cardiovascular system of a patient subjected to extracorporeal blood treatment.

EP 1 044 695 A2 teaches a method for determining the blood flow

rate in a vascular access during hemodialysis treatment. The method varies the blood flow rate of the extracorporeal circuit and measures the arterial and venous pressures in the extracorporeal circuit during the above-cited flow rate variations. The operations are carried out in two different conditions: first with the vascular access open, in which a part of the blood flow passes through the vascular access between the withdrawal needle and the return needle, and then when the vascular access is closed, in which the vascular access flow between withdrawal needle and return needle is zero. According to the method of EP 1 044 695 A2, vascular access blood flow rate, with the vascular access open, is judged to be equal to the blood pump flow rate at which the difference of arterial pressure (or venous pressure) in the two different situations is zero.

This method has the drawback that it is necessary to intervene mechanically on the fistula to interrupt blood flow.

WO 00/18451 teaches a method for determining the flow in a fistula of a patient using an extracorporeal blood flow circuit, such as for example a hemodialysis circuit, in which the blood flows from a withdrawal point in the fistula to a return point in the fistula. The method varies the blood flow rate in the extracorporeal circuit and takes a reading of a signal which can be correlated with the fistula flow rate downstream of the withdrawal point. The blood flow rate upstream of the withdrawal point is evaluated at equal the blood flow rate obtaining in the extracorporeal circuit when the fistula blood flow rate downstream, read with the above-described signal, is zero. WO 00/18451 includes an embodiment in which the signal which can be correlated to the fistula blood flow downstream of the withdrawal point is generated by an ultrasonic sensor which operates directly on the patient's vascular access.

The use of a sensor to directly measure the blood flow rate in the fistula tract comprised between the withdrawal needle and

the return needle leads to a certain constructional complication, as well as some discomfort for the patient.

EP 1 020 199 A2 teaches a method for detecting the presence of a stenosis in a vascular access during extracorporeal blood treatment. The method includes the use of at least one pressure sensor predisposed in the extracorporeal circuit along the arterial line upstream of the blood pump. A stenosis can be calculated from the entity of the pressure pulse measured by the pressure sensor.

A pressure sensor can be placed on the arterial line too downstream of the blood pump and upstream of a dialyzer, and a further pressure sensor can be placed on the venous line downstream of the dialyzer. The method also includes a reading of the pressure pulse frequency and use of that frequency as a signal entity correction factor. The pressure pulse frequency signal can be corrected by means of a function depending on the blood pump flow rate.

The data deductible from the method described in EP 1 020 199 A2 is however limited: in particular, the method provides only a general indication of the hemodynamic state of the fistula, signalling the presence of a stenosis, but it cannot gather more detailed data, such as for example the vascular access blood flow rate or the location of any stenoses found.

US 5,830,365 teaches a method for determining some hemodynamic parameters, among which the blood flow rate in a fistula during an extracorporeal blood treatment. The method involves the alteration of at least one chemical-physical characteristic of the blood in the venous line of the extracorporeal circuit, and recording the change which occurs in the arterial line following this alteration. The alteration can be a change in the concentration of an indicator, or a change in the temperature or pressure. In a specific embodiment use is made of a hemodialysis machine provided with a dialyzer where a dialysis solution containing an indicator flows and the concentration change of

the indicator in the venous and arterial lines of the extracorporeal circuit connected to the dialyzer is registered. In the venous line the concentration of the indicator increases by effect of back-filtration through the dialyzer. In the arterial line the concentration of the indicator increases by effect of recirculation in the fistula. The change of concentration in the arterial and venous lines is read by ultrasonic sensors. Alteration (in this case the change in concentration) is performed in two stages: first when the blood flows in the normal direction through the extracorporeal circuit, then when the blood flows in the opposite direction. The method includes the use of a device for inverting the blood flow direction in the extracorporeal circuit. According to the method taught in US 5,830,365 the change in concentration measured in the first stage enables calculation of recirculation at normal flow rate, while the change in concentration measured in the second stage enables calculation of recirculation when the flow is inverted. The two calculated values thus enable a calculation of various hemodynamic parameters among which the blood flow rate in the fistula.

However the alteration of the chemical-physical properties of the blood and the inversion of the flow during the course of extracorporeal treatment lead to various drawbacks: a constructional complication, a delay in carrying out the treatment, an invasive intervention on the blood, quite removed from the course of normal treatment.

WO 02/04044 teaches a method for identifying problems in arterial flow during an extracorporeal blood treatment in which the blood is transferred, by means of a positive displacement pump, from the vascular access of a patient to a blood treatment device through an arterial line and then sent by the treatment device to the vascular access through a venous line of the extracorporeal circuit. The method consists in measuring the amplitude of the periodic variations in pressure in the venous line induced by the rotation of the blood pump, by comparing the

variations with a threshold value and generating a control signal if the threshold value is exceeded. WO 02/04044 further describes another method according to which, during a dialysis treatment, the amplitude of the periodical variations of the pressure of the dialysis fluid (and not the venous line) is measured. The result is compared with a threshold value and if the threshold value is exceeded a control signal is generated.

The methods described in WO 02/04044 are not however able to provide data relating to the blood flow rate at the vascular access.

US 6,221,040 discloses a system for monitoring a vascular access during a dialysis treatment in which the pressures in both the arterial and venous branches of the extracorporeal blood system are monitored by pressure sensors. A computer unit generates first and second characteristic values for the integrity of the vascular access from measured arterial and venous pressures. An analyser unit analyses the integrity of the vascular access by comparing the first and second characteristic values to first and second ranges of predetermined values. Calculating a sum of the venous and arterial pressure generates the first characteristic value, and calculating a difference between the venous and the arterial pressure generates the second characteristic value.

The object of US 6,221,040 is to provide a monitoring system that allows detection of the venous cannula slipping out of the vascular access as well as detection of a blood leak in the venous branch of the extracorporeal circuit. It is not directed to determination of fistula flow.

US 5,866,015 and EP 0 773 035 disclose a method for determining hemodynamic parameters during an extracorporeal hemotherapy, including the steps of measuring the blood temperature in the arterial branch of the extracorporeal circuit, varying the blood flow in the extracorporeal circuit, storing the values of the extracorporeal blood flow and the measured values of the blood

temperature, and determining a value of the blood flow from the stored sequence of value pairs of blood temperature and of extracorporeal blood flow, at which value, after it is exceeded, the amount of the change in the blood temperature within a specific blood flow interval is greater than a predetermined limiting value. The fistula flow is inferred from the determined blood flow value.

The method is based on the fact that the measuring curve existing in discrete measured values is able to be represented by two subfunctions, the first subfunction indicating the blood temperature as a function of the extracorporeal blood flow for blood flow values smaller than the fistula flow or equal to the fistula flow, and the second subfunction indicating the blood temperature as a function of the blood flow for blood flow values greater than or equal to the fistula flow. The intersection of the two subfunctions indicates the point where the extracorporeal blood flow equals fistula flow. Thus, from the "break point" of the characteristic function curve, i.e., from the discontinuity in the rise of the curve, the point is able to be defined where fistula recirculation begins, i.e., where blood flow equals fistula flow.

In addition to measuring temperature, the concentration of a blood constituent (hematocrit) can also be measured, as can the density, speed of sonic propagation, optical density, and conductivity or viscosity.

The blood characteristic to be measured must have a different value in the venous branch of the extracorporeal circuit than it does in the blood flowing to fistula. It is assumed that the blood characteristic, preferably the temperature, is kept constant in the venous branch of the extracorporeal circuit while the measured values are recorded. If this characteristic is not constant, a regulating device to keep the characteristic in the venous branch constant must be provided. In the case of a temperature measurement, for example, this can be realized as a

temperature controller.

Another drawback of this method is that the delivery rate of blood pump, which predetermines the extracorporeal blood flow, is increased starting from a lower value to an upper limiting value which must be greater than the fistula flow to be expected. Fistula flows can only be determined within the adjustable blood flow range. Therefore the fistula flow is not determinable if it is equal to or greater than the upper limiting value of the adjustable blood flow range.

The prior art comprises the scientific publication entitled: "On-line dynamic measurement of fistula pressure during hemodialysis for detection of access stenosis and bad needle placement", Abstract from the 24th EDTNA-ERCA Conference, Prague, 5-8 July 1997, page 23, authors Polaschegg, Techert and Wizemann.

According to this publication it is possible to calculate the pressure of a vascular access by measuring the pressure in an extracorporeal blood circuit connected to the vascular access, with the aim of detecting any stenoses in the access itself.

In a scientific publication entitled "Dynamic pressure measurement for detection of blood access stenosis", published in the EDTNA-ERCA Journal, 1998, XXIV, 4, on pages 39-44, authors Polaschegg, Techert and Wizemann, more detail is given on monitoring problems in a patient's vascular access. The method is based on the determination of the venous and arterial pressures (upstream of the blood pump) in an extracorporeal blood circuit connected to the vascular access to be monitored. The method comprises a preliminary stage in which, through *in vitro* tests in which the extracorporeal circuit is not connected to a real vascular access, fluid resistances in the arterial and venous lines of the extracorporeal circuit are calculated. During a second stage the extracorporeal circuit is connected to the real vascular access of the patient in order to initiate an extracorporeal treatment. During the extracorporeal treatment

the venous and arterial pressures are calculated in the extracorporeal circuit. As the venous and arterial pressures in the extracorporeal circuit are known, as are the fluid resistances in the arterial and venous lines of the extracorporeal circuit, the pressures in the vascular access can be calculated. The dynamic measurement at different flow rates and the comparison with static measures enables stenoses at the vascular access to be identified.

The scientific publication entitled "Pressure drops in cannulas for hemodialysis", author H.D. Polaschegg, published in The International Journal of Artificial Organs, Vol. 24, No. 9, 2001, pp. 614-623, relates to a method for determining a fall in pressure in an arterial or venous line in hemodialysis, with which the vascular access pressures can be determined starting from the pressures measured in the extracorporeal circuit of the hemodialysis machine.

The scientific publication entitled "Extracorporeal pressure monitoring and the detection of vascular access stenosis", authors Kleinekofort, Kraemer, Rode and Wizemann, published in The International Journal of Artificial Organs, Vol. 25, No. 1, 2002, pp. 45-50, presents a method for identifying the presence of stenoses in a vascular access, even where the stenosis is located between the withdrawal needle and the return needle. The method comprises measuring the static pressures in the arterial and venous lines of an extracorporeal circuit and in calculating the pressures at the vascular access at the withdrawal point and the return point. These pressures, which correspond to the pressures which would be measured by two pressure sensors directly connected to the withdrawal and return needles, are used in order to identify the presence of a stenosis. A knowledge of the pressures both at the point of withdrawal and at the point of return of the vascular access provides more accurate indications and enables a first approximate localization of the stenosis, especially enabling to detect if the stenosis is in venous tract or is located between the

needles.

The method described here is not however able to determine the blood flow rate in the vascular access.

The publication entitled "Utility of intra-access pressure monitoring in detecting and correcting venous outlet stenoses prior to thrombosis", in Kidney International, Vol. 47 (1995), pages 1364-1373, authors Besarab, Sullivan, Ross, Moritz, teaches a method for deriving the pressure internally of the vascular access (intra-access pressure) from the pressure measured in the hemodialysis machine, as a function of the type of needle used, the blood flow rate of the hemodialysis machine, and the hematocrit of the blood. Other methods for determining the pressure at the vascular access are cited or described in the following publications:

- "Detection of access strictures and outlet stenoses in vascular accesses. Which test is best?", in ASAIO Journal, 1997, Vol. 43: pages M543-M547, authors Besarab, Lubkowski, Frinak, Ramanathan, Escobar;

- "Simplified measurement of intra-access pressure", in Journal of the American Society of Nephrology, 1998, Vol. 9, pages 284-289, authors Besarab, Frinak, Sherman, Goldman, Dumpler, Devita, Kapoian, Al-Saghir, Lubkowski;

- "Effect of systemic hemodynamics on flow within vascular accesses used for hemodialysis", in ASAIO Journal 2001, Vol. 47, pages 501-506, authors Besarab, Lubkowski, Vu, Aslam, Frinak;

- "Dynamic venous access pressure ratio test for hemodialysis access monitoring", in American Journal of Kidney Disease, Vol. 40, N° 4 (October), pages 760-768, 2002, authors Frinak, Zasuwa, Dunfee, Besarab, Yee.

An abstract entitled "A novel model-based method for monitoring the hemodialysis vascular access", published in the Journal of

the American Society of Nephrology, 2001, Vol. 12, N. A1513, pages 294A-295A, authors Lodi, Monari, Fava, Paolini, Grandi, Galato, Cavalcanti, cites a mathematical model based on the hemodynamic description of the vascular access which enables the arterial and venous pressures at the vascular access to be calculated and also the flow in vascular access starting from extracorporeal arterial and venous pressures. The model, which includes three parameters (resistance to flow of the anastomosis, resistance between arterial and venous access, the resistance which expresses the efficiency of venous circulation drainage), was used to analyse the data gathered during a normal hemodialysis therapy operation. The abstract states that the extracorporeal venous and arterial pressures were measured after having set four different flow rates on the blood pump and that the above-cited parameters included in the mathematical model were calculated using the mathematical model.

Summary of the Invention.

The present invention provides a system for controlling vascular access adequacy during an extracorporeal blood treatment.

An aim of the invention is to enable calculation of some hemodynamic parameters at the vascular access. Knowledge of these parameters enables both regulation of the blood pump flow rate operation in the extracorporeal circuit and intervention in case of detection of a pathological situation in the vascular access.

A further aim of the invention is to enable evaluation of the blood flow circulating in the vascular access of a patient during an extracorporeal blood treatment.

A further aim of the invention is to make available a system for evaluating vascular hydraulic resistance in various tracts of the patient's vascular system. In particular, an aim of the invention is to evaluate vascular resistance upstream of the blood withdrawal zone from the vascular access, downstream of

the blood return zone, and in the tract of vascular access comprised between the withdrawal zone and the return zone.

An advantage of the invention is that it provides indicative values of the efficiency of the vascular access simply, automatically, using devices (such as for example pressure transducers, blood pump, drainage pump) which are normally already present in machines for extracorporeal blood treatment. A further advantage is that the invention enables monitoring of the vascular access at any time during the extracorporeal blood treatment.

A further advantage of the invention is that the monitoring procedure does not cause extra stress to the patient. The procedure can be carried out by means of variations in the blood pump or the drainage pump flow rates, or both, within flow rate intervals which are normally compatible with the extracorporeal treatment the patient undergoes. The intervals can be those normally used during the course of therapy.

These aims and others besides are all attained by the invention as it is characterised in one or more of the appended claims.

In a special function of the invention, a mathematical model is used which contains at least two parameters in which a first parameter relates to the hemodynamics of the vascular access, and a second parameter relates to the blood flow rate in the extracorporeal circuit.

The mathematical model comprises a third parameter relating to at least one blood characteristic: this characteristic can be any physical, chemical or physical-chemical property thereof which characterises the blood in a vessel and which can be related to the blood flow rate in that vessel. A peculiarity of the invention is that the mathematical model used describes the relationship between the selected blood property (physical, chemical or physical-chemical) and the blood flow rate in the vessel. In particular the mathematical model describes the

relationship in the vascular access. For example, the mathematical model can describe the fluid-dynamic situation of the vascular access; the model can describe a relationship between the difference of pressure at two points of the vascular access and the flow rate crossing the points. Apart from the pressure it is also possible to select other properties (physical, chemical or physical-chemical) of the blood which are influenced by the flow rate, such as, for example: the difference in induced potential, speed of sound, optical characteristics, temperature, concentration of an indicator, and so on.

According to the invention, the monitoring of the vascular access is performed by varying the flow rate of at least one fluid (for example blood or the product of ultrafiltration), which runs either in the extracorporeal circuit or in at least one hydraulic line (for example an ultrafiltration line) connected to the extracorporeal circuit.

The monitoring can be carried out by varying both the above-cited flows.

The monitoring determines the values of at least one characteristic of the blood, in at least one zone of the blood circulation path, and at at least two different values of the flow rate of the fluid.

As mentioned above, the cited characteristic of the blood can be a physical, chemical or chemical-physical one. In an embodiment of the invention, among the various characteristics of the blood that depend on blood flow, the selected characteristic to be used is the pressure.

The monitoring procedure involves calculating one or more of the hemodynamic parameters of the vascular access contained in the mathematical model, using the values of the blood characteristic determined previously during the course of the procedure.

In an embodiment of the invention, a multiplicity of values of the blood characteristic is determined; then the said hemodynamic parameters are calculated, by means of the mathematical model, using approximation algorithms (of known type). The algorithms can be chosen, for example, from those which enable determination of the value of the hemodynamic parameter, by virtue of which the blood characteristic values calculated using the mathematical model, at different flow rate values, are those which are closest to the blood characteristic values which were previously determined during the course of the procedure, at the same flow rate values.

In an embodiment of the invention, the mathematical model used is descriptive of the pressure variation at the vascular access: it comprises at least one hemodynamic parameter relative to at least one characteristic of the vascular access; at least one parameter relative to the blood characteristic; and at least one parameter relative to the blood flow rate in the extracorporeal circuit.

The hemodynamic parameter can be relative to at least one of the following characteristics of the vascular access: the blood flow rate upstream of a withdrawal zone of the blood from the access, the blood flow rate between the withdrawal zone and a blood return zone at the access, the blood flow rate downstream of the blood return zone, the vascular hydraulic resistance upstream of the blood withdrawal zone from the access, the vascular hydraulic resistance between the blood withdrawal zone and the blood return zone, and the vascular hydraulic resistance downstream of the blood return zone.

In a further embodiment of the invention, the monitoring procedure includes determining the values assumed by the blood characteristic in at least two zones of the blood circulation path (where the blood circulation path comprises both the intracorporeal circuit and the extracorporeal circuit) and at at least two different flow rate values of one fluid (blood or the

product of ultrafiltration).

In a further embodiment of the invention, the monitoring procedure includes determining the values assumed by the blood characteristic in at least one zone of the blood circulation path and at at least two different flow rate values of two fluids (blood and the product of ultrafiltration).

In a further embodiment of the invention, the monitoring comprises a measuring stage of a blood characteristic, in a zone of the extracorporeal circuit arranged downstream of the blood withdrawal zone, or in a zone arranged upstream of the blood return zone, or in both above zones. The monitoring includes determining the blood characteristic in the vascular access, in the withdrawal zone, or in the return zone, or in both zones, by means of one or more mathematical models describing the variation of the said blood characteristic between the zones of withdrawal and return in the vascular access and the measuring zones in the extracorporeal circuit. The mathematical models can be, in particular, models descriptive of the variation of the said blood characteristic in the passage through the arterial or venous needles. In an embodiment of the invention, these mathematical models comprise at least one parameter which is relative to the blood flow, or at least one parameter relative to the hematocrit of the blood, or both said parameters. In particular the mathematical models can be represented by one or more interpolating formulas of experimental data; the formulas can be, for example, second-order polynomials with one or more parameters chosen between the flow rate and the hematocrit of the blood.

In a special operation of the invention, at regular time intervals the monitoring procedure determines the values assumed by the blood characteristic in at least one zone of the blood circulation path during the flow rate change, evaluates the variation of the blood characteristic, selects the values assumed by the blood characteristic when the variation has

exceeded a threshold limit value, and uses the selected values to calculate the value of the blood characteristic at the vascular access.

In a further special operation of the invention, at regular time
5   intervals the monitoring procedure determines the values of the blood characteristic in two different zones of the blood circulation path during flow rate change, compares the variation of the blood characteristic detected in a first zone of the blood circulation path and the variation of the characteristic
10   detected in a second zone thereof, selects the values of the blood characteristic when the difference between the variations has exceeded a threshold limit value, and uses the selected values in calculating the value of the blood characteristic at the vascular access.

15   In another characteristic of the invention, in calculating the value of the characteristic of the vascular access, the monitoring procedure considers the values of the blood characteristic in a stationary blood flow situation, i.e. after having kept the flow rate constant for a determined period of
20   time.

The monitoring procedure is applied by means of a machine for blood treatment in an extracorporeal circuit, in particular for a machine for treatment of kidney failure, predisposed to perform one or more of the following therapies: hemodialysis,
25   hemofiltration, hemodiafiltration, pure ultrafiltration, plasmapheresis.

The machine is provided with a timer for carrying out the monitoring procedure at least once during the extracorporeal treatment.

30   The monitoring procedure can be initiated on command of an operator, or automatically at a predetermined moment during the treatment.

The extracorporeal circuit can be included in the complex of fluid distribution lines, of the disposable type, normally removably associated and used in a machine for treatment of renal failure.

The machine is normally equipped with pressure transducers operating in the blood withdrawal line, before the blood pump, and in the blood return line, after the blood treatment unit.

Further characteristics and advantages of the present invention will better emerge from the detailed description that follows, of a specific embodiment of the invention, illustrated purely in the form of a non-limiting example in the figures of the drawings.

Brief Description of the Drawings.

The description will be made herein below with reference to the appended figures of the drawings, here given by way of non-limiting illustration, in which:

- figure 1 is a diagram of a machine for an extracorporeal blood treatment provided with a monitoring device of the vascular access according to the invention;

- figure 2 is a diagram of blood flow in a patient connected up to the machine of figure 1;

- figure 3 is an electrical diagram which describes by analogy the circulation of extracorporeal and intracorporeal blood of the patient subjected to the extracorporeal treatment with the machine of figure 1;

- figure 4 shows a diagram of the relation between ΔP_f and q_b, where $\Delta P_f = P_{af} - P_{vf}$ (difference between arterial pressure in the vascular access P_{af} and venous pressure in the vascular access P_{vf}) and q_b is the extracorporeal flow rate of the blood;

- figure 5 is a diagram of the relation between $(P_{vf} - P_v)$ e q_{uf}, where $(P_{vf} - P_v)$ is the difference between the venous pressure in the vascular access P_{vf} and the systemic venous pressure P_v, and q_{uf} is the ultrafiltration flow rate.

Detailed Description.

The machine illustrated in figure 1 is a machine for hemodiafiltration comprising a unit for an extracorporeal blood treatment (a filter for hemodiafiltration 1) having two chambers 2, 3 separated by a semipermeable membrane 4. A first chamber 2 has an inlet which is connected to an arterial line 5 (blood withdrawal line from the patient) of an extracorporeal blood circuit. The arterial line 5 is connectable with a vascular access 6 of a patient by means of an access tool constituted in the example by an arterial needle N_A. The arterial line 5 is provided with a pressure sensor 8 and a positive displacement pump 9 for blood circulation along the extracorporeal circuit in the direction of the arrow 7.

The first chamber 2 has an outlet connected to a venous line 10 (blood return line to the patient) of the extracorporeal blood circuit. The venous line 10 is connectable to the vascular access 6 of the patient by means of an access tool constituted in the illustrated embodiment by a venous needle N_v. The venous line 10 is provided with a pressure sensor 12.

The second chamber 3 of the filter 1 has an inlet connected to a supply line 14 of a fresh treatment fluid (dialysis liquid) and an outlet connected to a discharge line 15 of a discharge fluid (the dialysis liquid and the ultrafiltered liquid). The supply line 14 is provided with a supply pump 13 of the fresh treatment fluid. The discharge line 15 is provided with a drainage pump 16 for the circulation of the discharge fluid in the direction of the arrow 11.

The dialysis machine further comprises a control and calculation unit 17 connected to a screen and also to a keyboard through

which the user communicates to the control and calculation unit the setting values for machine operation. One of the setting values which the control and calculation unit 17 receives from the user is the blood flow rate q_b in the arterial blood withdrawal line 5. The control and calculation unit 17 can control the speed of the blood pump 9 in order to have the predetermined value of flow rate q_b. The control and calculation unit 17 can be connected to at least one measuring device, able to provide information relating to the effective blood flow rate in the arterial line. The measuring device can comprise, for example, a flowmeter, or an encoder connected to the rotor of a blood pump. The control and calculation unit 17 is further connected to the pressure sensors 8 and 12 and receives therefrom the signals indicating the detected pressure.

The control and calculation unit 17 controls the operation of the various motor devices of the machine, in particular the blood pump 9 and drainage pump 16, according to the instructions received from the user and the programmed algorithms contained in its memory.

The machine can further comprise sensors (of known type and not illustrated) for detecting the blood viscosity upstream and downstream of the treatment unit 1. The sensors can comprise, for example, measuring devices for the blood hematocrit level.

The control and calculation unit is programmed to carry out, automatically or by request of the user, a series of operations which enable the vascular access to be monitored.

Figure 2 shows the patient's blood circulation subjected to extracorporeal treatment with the machine of figure 1. The vascular access 6, through which the extracorporeal blood circuit is connected to the cardio-vascular circuit of the patient is, in the embodiment, a fistula of the Cimino-Brescia type. In figure 2 H indicates the patient's heart, P denotes the pulmonary circuit, V denotes the vascular system (or systemic circuit, or intravascular circuit or intracorporeal circuit).

The arterial line 5 and the venous line 10 are connected at one end to the vascular access 6 and at the other end to the dialysis filter 1.

Figure 3 shows an electrical diagram which, by analogy, describes the blood circulation of the patient subjected to the extracorporeal blood treatment.

The legend to figure 3 is as follows.

Quantities controlled by the control unit 17:

q_b blood pump flow rate [ml/min]

q_{uf} ultrafiltration flow rate [ml/min]

Known quantities (measurable directly or indirectly or determinable from indirect measurements using a mathematical model):

P_{am} extracorporeal arterial pressure [mmHg]

P_{vm} extracorporeal venous pressure [mmHg]

E_{art} hydrostatic pressure related to the height level difference between the pressure sensor 8 in the arterial line of the extracorporeal circuit and the arterial needle N_A [mmHg]

E_{ven} hydrostatic pressure related to the height level difference between the pressure sensor 12 in the venous line of the extracorporeal circuit and the venous needle N_V [mmHg]

R_{am} hydraulic resistance of the extracorporeal arterial line [mmHg·min/ml]

R_{vm} hydraulic resistance of the extracorporeal venous line [mmHg·min/ml]

P_{af} vascular access arterial pressure [mmHg]

P_{vf} vascular access venous pressure [mmHg]

P_a mean systemic arterial pressure (MAP) [mmHg]

P_v venous pressure (venous return pressure) [mmHg]

Unknown quantities to be determined:

q_a blood flow rate at the vascular access, upstream of the
         arterial access [ml/min]

q_f blood flow rate of artero-venous anastomosis in the
         vascular access tract comprised between the arterial access
         and the venous access, ($q_f = q_a - q_b$) [ml/min]

q_v blood flow rate downstream of the venous access, ($q_v = q_a -$
         q_{uf}) [ml/min]

R_d hydraulic resistance upstream of the vascular access
         [mmHg·min/ml]

R_f hydraulic resistance between the arterial access and the
         venous access [mmHg·min/ml]

R_v hydraulic resistance downstream of the vascular access
         [mmHg·min/ml]

In the diagram of figure 3 the extracorporeal blood circuit is
traced in bold line, while the intracorporeal circulation in the
vascular access is drawn in thin line.

The nodes where the extracorporeal circuit meets with the
vascular access are the zones where pressures P_{af} e P_{vf} are
determined (either directly measured or calculated).

Various methods are known, based on mathematical models, for
calculating pressures P_{af} e P_{vf} from known pressures P_{am} e P_{vm} in
the extracorporeal circuit. Some of these methods are described
in the scientific publications cited in the present description.
Herein below details will be given of a method founded on a new
mathematical model based on the electrical diagram represented
in figure 3.

In the following a mathematical model is shown, also based on the electrical diagram of figure 3, representative of the hemodynamics of the vascular access of an extracorporeal blood circuit in which the blood is removed from the patient through an arterial needle, is made to circulate through the extracorporeal circuit and is returned through a venous needle.

The mathematical model describes the variation of pressure in the vascular access as a function of the blood flow rate.

The mathematical model is expressed in the following three equations which can be derived from the electrical diagram represented in figure 3.

$$q_a = \frac{P_a - P_{af}}{R_d}$$

$$P_{af} - P_{vf} = R_f \cdot (q_a - q_b)$$

$$P_{vf} - P_v = R_v \cdot (q_a - q_{uf})$$

where, as mentioned herein above, the symbols have the following meanings:

q_a = blood flow rate at the vascular access 6 (fistula), upstream of the withdrawal point of the arterial needle N_A

q_b = blood flow rate in the arterial line 5 of the extracorporeal circuit

P_a = mean systemic arterial pressure measured at patient's arm

P_{af} = arterial pressure in the vascular access 6, i.e. the pressure in the vascular access (in the embodiment, with a Cimino-Brescia fistula, this is a tract of arterialized vein) at the point of withdrawal of the arterial needle N_A

R_d = resistance of the tract of arterialised vein comprised between the anastomosis and the point of withdrawal of the arterial needle N_A

P_{vf} = venous pressure in the vascular access 6, i.e. the pressure in the fistula at the return point of the venous needle N_v

R_f = vascular resistance of the tract of fistula comprised between the two needles N_A and N_v and representing the resistance between the two points at which P_{af} and P_{vf} are determined

P_v = venous pressure of the blood in the distal venous branch; the Pv value can be unknown during the extracorporeal treatment; in this case it can be placed at a constant physiological value (e.g. P_v = 0)

R_v = vascular resistance in the venous branch of the blood return zone at the zone where venous pressure P_v is evaluated; where P_v = 0, the resistance R_v represents total venous resistance, i.e. the vascular resistance met by the blood in returning from the venous needle N_v to the heart H, which constitutes an indicative value of the drainage efficiency of the venous circulation

q_{uf} = ultrafiltration flow rate (in case of hemodiafiltration, q_{uf} is the difference between the discharge fluid flow rate in the discharge line 15 and the fresh dialysis fluid flow rate in the supply line 14).

The pressures in the above-indicated mathematical model relate to atmospheric pressure. The arterial and venous pressures P_{af} and P_{vf} in the vascular access are measurable directly, for example using pressure sensors operating directly on the vascular access 6 in proximity or internally of the arterial and venous needles N_A e N_v.

As previously mentioned, the pressures P_{af} and P_{vf} are also determinable indirectly using a mathematical model which includes, among its parameters, pressures P_{am} and P_{vm} (arterial and venous pressures) measured in the extracorporeal circuit by

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the pressure sensors 8 and 12. The prior art comprises various mathematical models usable for calculating pressures P_{af} and P_{vf} when pressures P_{am} and P_{vm} are known. Some of the above-cited prior art contains examples of so-usable mathematical models. There follows a further example of a mathematical model usable for determining the intravascular pressures of the blood starting from the easily-measurable values of the extracorporeal blood pressures.

Determination of P_{af} and P_{vf} with P_{am} and P_{vm} known.

The mathematical model used comprises the two equations which can be derived from the electrical diagram of figure 3:

$$P_{af} = P_{am} + E_{art} + R_{am} \cdot q_b$$

$$P_{vf} = P_{vm} + E_{ven} - R_{vm} \cdot \left(q_b - q_{uf}\right)$$

Resistances R_{am} and R_{vm} can be considered equal, with satisfactory approximation, to the hydraulic resistance of the arterial needle N_A and, respectively, the venous needle N_V; it is therefore assumed for the sake of simplicity that the whole drop in pressure in the arterial and venous lines is concentrated at the respective needles.

To calculate the hydraulic resistance R of a needle, the following mathematical model is used: it makes use of an equation which connects the hydraulic resistance of the needle with the blood flow rate and the blood hematocrit.

$$R = \left(A_2 \cdot q_b^2 + A_1 \cdot q_b + B_2 \cdot Hct^2 + B_1 \cdot Hct + B_0\right) \cdot R_{Poiseuille}$$

where

q_b = blood flow rate

Hct = blood hematocrit

$$R_{Poiseuille} = \frac{8 \cdot L}{\pi \cdot r^4}$$

L = length of needle

r = radius of internal section of the needle

$R_{Poiseuille}$ is the theoretical hydraulic resistance calculated using the Hagen-Poiseuille law for a liquid with viscosity equal to one.

A_2, A_1, B_2, B_1 and B_0 are coefficients characteristic of each needle, the value being obtained by means of experimental preliminary laboratory testing, by measuring the fall of pressure through the needle with different blood and hematocrit flow rates. In experimental tests the flow rate was varied within a range from 0 to 500 ml/minute, while the hematocrit was varied within a range from 30 to 45%. The coefficients differ for a same needle according to blood flow direction, that is whether the needle is used as an arterial needle or as a venous needle. These preliminary *in vitro* tests serve to experimentally characterise the needles which will then be used for the extracorporeal blood treatment. The tests include simulation of the extracorporeal treatment (for example dialysis) using a machine for performing the treatment (for example a dialysis machine) with an extracorporeal circuit lacking the device for effecting the treatment (for example lacking a dialyzer filter), causing bovine blood to circulate, exiting from a container and returning thereto. The blood is kept at a constant temperature of 37°C. The blood hematocrit is measured. The machine and the circuit used in the tests can be the same as those illustrated in figure 1.

At intervals of about 1 minute the blood pump flow rate q_b is changed, starting from a zero flow rate q_{b0} = 0 ml/minute and increasing it by 50 ml/minute up to a maximum flow rate of 500 ml/minute (q_{b1}=50ml/min, q_{b2}=100ml/min, …, q_{bi}=i·50ml/min, …, q_{b10}=500ml/min). In general, the flow rate q_b assumes N different values q_{bi} with i = 0, 1, 2, …, N (N ≥ 3).

At each interval pressures P_{ami} and P_{vmi} are measured using the

pressure sensors placed along the extracorporeal circuit. From each pressure value measured, P_{ami} and P_{vmi}, we subtract the hydrostatic pressure due to the different blood level in the container with respect to the point of measurement of the pressure on the machine. From pressures P_{ami} and P_{vmi} we can deduce the pressure falls of the corresponding needles ΔP_{ai} and ΔP_{vi}, with i = 0, 1, 2, …, N (N ≥ 3).

The same operations are repeated, each time controlledly changing the value of the hematocrit in the bovine blood. The blood flow rate values q_b are the same each time, i.e. $q_b = q_{bi}$, with i = 0, 1, 2, …, N.

The hematocrit can be varied by dilution with physiological solution (in this case the hematocrit diminishes each time). For each series of operations the value of the hematocrit is measured. Purely by way of an example, the operations can be performed with the following hematocrit values: about 44%, about 42%, about 40%, about 38%, about 36%, about 34%, about 32 %. In general the value of the hematocrit Hct assumes M different Hct_j values with j = 1, 2, …, M (with M ≥ 2).

Thus, for each needle we obtain a number N·M of values ΔP_{aij} and ΔP_{vij} with i = 0, 1, 2, …, N (with N ≥ 3) e j = 1, 2, …, M (with M ≥ 2).

A processor calculates the hydraulic resistances of the needle, normalised with respect to the Poiseuille resistance, for one of the hematocrit values (for example Hct = Hct_1) according to the equation:

$$R_{ai1} = \frac{\Delta P_{ai1}}{q_{bi}} \cdot \frac{1}{R_{Poiseuille}}$$

$$R_{vi1} = \frac{\Delta P_{vi1}}{q_{bi}} \cdot \frac{1}{R_{Poiseuille}}$$

in which

R_{ai1} = resistance of the arterial needle at flow rate $q_b = q_{bi}$ and with hematocrit Hct = Hct_1

R_{vi1} = resistance of the venous needle at flow rate $q_b = q_{bi}$ and with hematocrit Hct = Hct_1

5   ΔP_{ai1} = pressure drop on the arterial needle at flow rate $q_b = q_{bi}$ and with hematocrit Hct = Hct_1.

ΔP_{vi1} = pressure drop on the venous needle at flow rate $q_b = q_{bi}$ and with hematocrit Hct = Hct_1.

Hence we obtain two series of values R_{ai1} and R_{vi1} of resistances

10   (one arterial and the other venous) corresponding to a determined hematocrit value (in the example Hct = Hct_1), with i = 0, 1, 2,…, N, with N = number of times we determine ΔP_{ai1} and ΔP_{vi1} at different flow rates q_{bi}.

Each of the two series of values (R_a and R_v) is interpolated by

15   the processor using a second-order polynomial:

$$R = A_2 q_b^2 + A_1 q_b + b_1$$

and we thus obtain, for each type of needle, a pair of coefficients A_2 and A_1 for each flow direction (i.e. we obtain a pair of coefficients which characterise the arterial needle and

20   a pair of coefficients which characterise the venous needle). Coefficient b_1 depends on the blood hematocrit value.

Coefficients B_2, B_1 and B_0 are obtained as follows.

Let us for a moment consider only one blood flow direction through the needle: for example, the arterial needle.

25   The processor also calculates the resistances R_a of the arterial needle for the other hematocrit values Hct = Hct_j (j = 2,…, M), at different blood flow rates $q_b = q_{bi}$ (i = 0, 1, 2,…, N), thus obtaining various series of values:

$$R_{aij} = \frac{\Delta P_{aij}}{q_{bi}} \cdot \frac{1}{R_{Poiseuille}}$$

These values of R_a are interpolated, for each hematocrit value Hct, according to the blood flow rate q_b, using a second order polynomial:

5
$$R_{ai2} = A_2 q_b^2 + A_1 q_b + b_2 \quad \text{for Hct} = \text{Hct}_2$$

$$R_{ai3} = A_2 q_b^2 + A_1 q_b + b_3 \quad \text{for Hct} = \text{Hct}_3$$

$$R_{aiM} = A_2 q_b^2 + A_1 q_b + b_M \quad \text{for Hct} = \text{Hct}_M$$

with i = 0, 1, 2, ..., N (with N ≥ 3), in order to obtain a series
10 of values b_j (j = 1, 2,..., M).

In substance, exemplifying the above-mentioned process step by step, for j = 1 the processor interpolates values R_{ai1} (for Hct = Hct_1) according to the equation

$$R_{ai1} = A_2 q_b^2 + A_1 q_b + b_1$$

15 and thus determines b_1.

Then it interpolates values R_{ai2} for j = 2 (for Hct = Hct_2) following the equation

$$R_{ai2} = A_2 q_b^2 + A_1 q_b + b_2$$

and determines b_2, and so on up until j = M, thus obtaining M
20 values of b_j.

At this point the processor makes a further interpolation, using the values of b_j according to the equation

$$b = B_2 Hct^2 + B_1 Hct + B_0$$

and thus determines coefficients B_2, B_1 and B_0.

The same series of interpolations is effected using the data relating to the venous needle.

Hereafter we report some examples of values of the coefficients A_2, A_1, B_2, B_1 and B_0 experimentally obtained.

5   With a needle having the following characteristics: gauge = 15 (internal diameter = 1.6mm), length = 28mm, the following is obtained:

A_2(arterial) = -0.00004, A_1(arterial) = 0.0351,

B_2(arterial) = 0.0192, B_1(arterial) = -0.9398,

10   B_0(arterial) = 21.059, $R_{Poiseuille}$ = 0.022

A_2(venous) = -0.000026, A_1(venous) = 0.0266, B_2(venous) = 0.0403, B_1(venous) = -2.2937, B_0(venous) = 41.969, $R_{Poiseuille}$ = 0.022

With a needle having the following characteristics: gauge = 16 (internal diameter = 1.4mm), length = 33mm, the following is

15   obtained:

A_2(arterial) = -0.00004375, A_1(arterial) = 0.0309,

B_2(arterial) = 0.0081, B_1(arterial) = -0.3226,

B_0(arterial) = 8.3882, $R_{Poiseuille}$ = 0.0442

A_2(venous) = -0.00002875, A_1(venous) = 0.0193,

20   B_2(venous) = 0.0037, B_1(venous) = 0.0487,

B_0(venous) = 1.4565, $R_{Poiseuille}$ = 0.0442.

The control and calculation unit 17 memory is preloaded with the coefficient values A_2, A_1, B_2, B_1 and B_0 of the most commonly used needles (the memory contains two series of coefficients for each

25   needle, one for each blood flow direction, i.e. a series relating to a needle's use as an arterial needle and as a venous needle). The control and calculation unit 17 recognises the

needle used in the extracorporeal treatment time by time and consequently in the calculation of P_{af} and P_{vf} uses the coefficients relating to the needle being used. Recognition of the needle can be automatic (for example by means of an identification system associated to the needle) or can be user-guided.

Thus a mathematical model is defined, usable by the control and calculation unit 17 for determining the pressures in the vascular access by measuring the pressure in the extracorporeal circuit.

Herein below some operative methods are defined by means of which a processor in the control and calculation unit 17 of the machine can monitor the vascular access during an extracorporeal treatment.

First monitoring procedure.

In this first operative mode q_b is varied at q_{uf} = constant (= 0), while P_{am} and P_{vm} are measured.

The operative mode is now described step by step.

a. Determine values P_{af1} and P_{vf1} of the arterial pressure and, respectively, the venous pressure in the vascular access (fistula) at a known blood pump flow rate q_{b1}.

b. Save and store values q_{b1}, P_{af1} and P_{vf1} in a memory.

c. Change the blood pump flow rate to a known value q_{b2}. At the same time the ultrafiltration flow rate q_{uf} is kept constant.

d. Keep the blood pump flow rate at q_{b2} for a determined period of time (for example about ten seconds) to let the system become stable.

e. Determine values P_{af2} and P_{vf2} of the arterial pressure and, respectively, of the venous pressure in the vascular access

(fistula) at blood pump flow rate q_{b2}.

f.   Save and store values q_{b2}, P_{af2} and P_{vf2}.

g.   Steps c-f can be repeated for a desired number of times so as to save and store a series of values q_{bi}, P_{afi}, P_{vfi}, with i = 1, 2, 3, …, N, where N is an integer number greater than 1.

h.   Calculate R_f and q_a using the values stored in the memory and the mathematical model expressed by the equation

$$P_{af} - P_{vf} = R_f \cdot (q_a - q_b)$$

i.   Save and store the values calculated for R_f and q_a.

j.   Calculate R_v using at least a part of the stored values and the mathematical model expressed by the equation

$$P_{vf} - P_v = R_v \cdot (q_a - q_{uf})$$

k.   Save and store the calculated value for R_v.

l.   Calculate R_d using at least a part of the stored values and the mathematical model expressed in the equation

$$q_a = \frac{P_a - P_{af}}{R_d}$$

where P_a (mean systemic arterial pressure or MAP) is measured at the patient's arm in known ways and the measured value of P_a is transmitted to the control and calculation unit 17.

m.   Save and store the value calculated for R_d.

The calculation of R_f and q_a in point h can be done in the following way.

The stored values of q_{bi}, P_{afi} and P_{vfi}, with i = 1, 2, …, N (with N ≥ 2), are introduced into the equation

$$P_{af} - P_{vf} = R_f \cdot (q_a - q_b)$$

so as to obtain a system of N equations with 2 unknowns q_a and R_f.

$$\Delta P_{f1} = R_f \cdot (q_a - q_{b1})$$

$$\Delta P_{f2} = R_f \cdot (q_a - q_{b2})$$

...

$$\Delta P_{fN} = R_f \cdot (q_a - q_{bN})$$

where $\Delta P_{fi} = P_{afi} - P_{vfi}$ with $i = 1, 2, ..., N$ ($N \geq 2$)

The unknown quantities q_a and R_f can be determined by calculating the optimal solution of the above-indicated equation system.

If $N = 2$ the system has an analytical solution.

If $N > 2$ the two unknowns q_a and R_f can be determined using an optimisation algorithm.

For example the processor calculates the two values, one q_a and the other R_f, for which the corresponding values of ΔP_f calculated by the above-indicated system of equations are the closest to the ΔP_{fi} values previously determined at point e.

The following calculation procedure can be used. Using the values stored in memory, q_{bi}, P_{afi} and P_{vfi}, by means of a mathematical interpolation algorithm previously stored in memory the processor determines a linear equation which approximates the relation between ΔP_f and q_b. Then the value of q_b at $\Delta P_f = 0$ is calculated, using the above-indicated linear equation. The value of q_b at $\Delta P_f = 0$ is assumed to be equal to the flow rate q_a of the vascular access. The value of q_a thus determined is stored in memory. Further, the processor calculates the value assumed by ΔP_f at $q_b = 0$, once more using the same linear equation. The value of ΔP_f at $q_b = 0$ is assumed to be equal to the product of $R_f \cdot q_a$. At this point, using the previously-stored

value of q_a the value of R_f can be calculated with a simple quotient.

Graph $\Delta P_f - q_b$ of figure 2 illustrates this mode of procedure. The points in figure 2 represent the determined values ΔP_{fi} of ΔP_f according to the blood pump flow rate q_b. The straight line interpolating the various points is the graphic representation of the linear mathematical relation which connects ΔP_f with q_b.

The interpolation method can be any known linear interpolation method. The straight line of interpolation intersects the horizontal axis (q_b) at q_a and the vertical axis (ΔP_f) at $R_f \cdot q_a$.

Another way of calculating q_a and R_f is based on the description of the relation between q_b and ΔP_f using a non-linear mathematical relation (for example a polynomial of a degree greater than one), derived by the processor with an interpolation method using the values stored in the memory q_{bi}, P_{afi} e P_{vfi}. After having derived this non-linear relation, the value assumed by q_b at $\Delta P_f = 0$ is assumed to be equal to the flow rate q_a of the vascular access. The value of q_a thus determined is stored in memory. Further, the processor calculates the value assumed by ΔP_f at $q_b = 0$, using the above-cited non-linear equation as well. The value of ΔP_f at $q_b = 0$ is assumed to be equal to the product of $R_f \cdot q_a$. At this point, using the previously-stored value of q_a it is possible to calculate, by a simple division, the value of R_f. This value represents, in the embodiment, the value of hydraulic resistance R_f at point $q_b = 0$ (i.e. at zero blood flow rate in the extracorporeal circuit).

At point c., the blood pump flow rate is varied from q_{b1} to q_{b2} so that, in consequence of the change of flow rate $q_{b2} - q_{b1}$, the pressure difference $\Delta P_f = P_{af} - P_{vf}$ varies significantly in absolute value and sufficiently to be appreciated (for example at least 2 mmHg), i.e. so that

$$\left| \Delta P_{f1} - \Delta P_{f2} \right| \geq 2 \text{ mmHg,}$$

where

$$\Delta P_{f1} = P_{af1} - P_{vf1} \text{ and}$$

$$\Delta P_{f2} = P_{af2} - P_{vf2}$$

The same occurs for each flow rate change from q_{bi} to $q_{b(i+1)}$. The
5   values of q_{bi} are selected so that the difference between the
minimum value and the maximum value of q_{bi} does not exceed a
predefined value (for example about 600 ml/min) in order that q_a
and R_f can be considered as constant in the calculation with good
approximation.

10 At point c. the ultrafiltration flow rate q_{uf} is kept constant =
0.

At point j. the resistance R_v is calculated assuming $q_{uf} = 0$. The
R_v stored in memory can be one of the estimated R_{vi} or the mean
value of the estimated R_{vi}.

15
$$R_{vi} = \frac{P_{vfi} - P_v}{q_a}$$

At point l. the resistance R_d stored in the memory can be one of
the R_{di} calculated with equation (1) or the mean value of the
calculated R_{di}.

$$R_{di} = \frac{P_a - P_{afi}}{q_a}$$

20 **Second monitoring procedure.**

In the second operative mode q_{uf} is changed to q_b = constant (not
zero), while P_{am} and P_{vm} are measured.

The operative mode is now described step by step.

a.   Determine values P_{af1} and P_{vf1} of the arterial pressure and,
25   respectively, of the venous pressure in the vascular access
         (fistula) at a known ultrafiltration flow rate q_{uf1} at a

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predetermined blood pump flow rate q_b.

b.   Save and store values q_{uf1}, P_{af1} and P_{vf1}.

c.   Change the ultrafiltration flow rate to a known value q_{uf2}. At the same time the blood pump flow rate q_b is kept constant and equal to the initial flow rate of point a..

d.   Keep the ultrafiltration pump flow rate at value q_{uf2} for a determined period of time (for example about ten seconds) to let the system become stable..

e.   Determine values P_{af2} and P_{vf2} of the arterial pressure and, respectively, the venous pressure in the vascular access (fistula) at ultrafiltration flow rate q_{uf2} of the blood pump.

f.   Save and store values q_{uf2}, P_{af2} and P_{vf2}.

g.   Steps c-f can be repeated for a desired number of times so as to save and store a series of values q_{ufi}, P_{afi}, P_{vfi}, with i = 1, 2, 3, …, N, where N is an integer number greater than 1.

h.   Calculate q_a and R_v using the values stored in the memory and the mathematical model expressed in the equation

$$P_{vf} - P_v = R_v \cdot \left(q_a - q_{uf} \right)$$

i.   Save and store the values calculated for R_v and q_a.

j.   Calculate R_f using at least a part of the stored values and the mathematical model expressed in the equation

$$P_{af} - P_{vf} = R_f \cdot \left(q_a - q_b \right)$$

k.   Save and store the calculated value for R_f.

l.   Calculate R_d using at least a part of the stored values and the mathematical model expressed in the equation

$$q_a = \frac{P_a - P_{af}}{R_d}$$

m.   Save and store the value calculated for R_d.

At point c., the ultrafiltration flow rate is changed from q_{uf1} to q_{uf2} so that, in consequence of the change in flow rate $q_{uf2} - q_{uf1}$, the difference of pressure $\Delta P_{vf} = P_{vf} - P_v$ significantly varies in absolute terms sufficiently to be appreciated (for example at least 3 mmHg), i.e. so that

   $\left| \Delta P_{vf1} - \Delta P_{vf2} \right| \geq$ 3 mmHg,

where

   $\Delta P_{vf1} = P_{vf1} - P_v$ and

   $\Delta P_{vf2} = P_{vf2} - P_v$

The same can be said for each flow rate change from q_{ufi} to $q_{uf(i+1)}$.

At point c. the blood flow rate in the extracorporeal circuit q_b is kept constant at a known value which is not zero.

At point h. the calculation of R_v and q_a is performed in the following way.

The stored values of q_{ufi}, P_{afi} and P_{vfi}, with i = 1, 2, ..., N (with N ≥ 2), are introduced in the equation

$$P_{vf} - P_v = R_v \cdot \left(q_a - q_{uf} \right)$$

so as to obtain a system of N equations with 2 unknown quantities q_a and R_v .

$$P_{vf1} - P_v = R_v \cdot \left(q_a - q_{uf1} \right)$$

$$P_{vf2} - P_v = R_v \cdot \left(q_a - q_{uf2} \right)$$

   ...

$$P_{vfN} - P_v = R_v \cdot \left(q_a - q_{ufN} \right)$$

The unknown quantities q_a and R_v can be determined by calculating the optimal solution of the above-indicated equation system.

If N = 2 the system has an analytical solution.

If N > 2 the two unknowns q_a and R_v can be determined using an optimization algorithm.

A calculation procedure which can be used is the following. Using the values stored in memory, q_{ufi} and P_{vfi}, the processor determines, by means of a mathematical interpolation algorithm previously stored in memory, a linear equation which approximates the relation between ΔP_{vf} and q_{uf} where $\Delta P_{vf} = P_{vf} - P_v$. Then the value assumed by q_{uf} at $P_{vf} - P_v = 0$ is calculated, using the above-indicated linear equation. The value of q_{uf} at $\Delta P_{vf} = 0$ is assumed to be equal to the flow rate q_a of the vascular access. The value of q_a thus determined is stored in memory. Further, the processor calculates the value assumed by ΔP_{vf} at $q_{uf} = 0$, once more using the same linear equation. The value of ΔP_{vf} at $q_{uf} = 0$ is assumed to be equal to the product of $R_v \cdot q_a$. At this point, using the previously-stored value of q_a the value of R_v can be calculated by a simple division.

The plot of ΔP_{vf} as a function of q_{uf} in figure 5 illustrates this mode of procedure. The points in figure 5 represent the determined values $\Delta P_{vfi} = P_{vfi} - P_v$ of ΔP_{vf} as functions of the ultrafiltration pump flow rate q_{uf}. The straight line interpolating the various points is the graphic representation of the linear mathematical relation which connects ΔP_f with q_{uf}. The interpolation method can be any known linear interpolation method. The straight interpolating line intersects the horizontal axis q_{uf} at q_a and the vertical axis of ΔP_{vf} at $R_v \cdot q_a$.

At point j. (determination of R_f) the following procedure is observed.

For each of the estimated values of P_{afi} and P_{vfi}, a corresponding

value of R_{fi} is calculated using the above-indicated equation, from which it is obtained:

$$R_{fi} = \frac{P_{afi} - P_{vfi}}{q_a - q_{b1}}$$

The R_f value stored at point k. can be one of the calculated values for R_{fi} or the mean value of the R_{fi} values.

At point 1. (determination of R_d) the following procedure is observed.

For each of the estimated values of P_{afi}, a corresponding value of R_{di} is calculated using the above-indicated equation:

$$R_{di} = \frac{P_a - P_{afi}}{q_a}$$

The R_d value stored at point 1. can be one of the calculated values R_{di} or the mean value of the R_{di} values.

Third monitoring procedure.

The equations which define the mathematical model of the vascular access used previously:

$$q_a = \frac{P_a - P_{af}}{R_d}$$

$$P_{af} - P_{vf} = R_f \cdot (q_a - q_b)$$

$$P_{vf} - P_v = R_v \cdot (q_a - q_{uf})$$

can be reformulated so as to evidence the dependence of P_{af} and P_{vf} on P_a, q_b, q_{uf} and P_v through the unknown parameters R_d, R_f and R_v. The reformulated equations are as follow:

$$P_{af} = \frac{R_f + R_v}{R_d + R_f + R_v} \cdot P_a - \frac{R_d \cdot R_f}{R_d + R_f + R_v} \cdot q_b - \frac{R_d \cdot R_v}{R_d + R_f + R_v} \cdot q_{uf} + \frac{R_d}{R_d + R_f + R_v} \cdot P_v$$

$$P_{vf} = \frac{R_v}{R_d + R_f + R_v} \cdot P_a + \frac{R_f \cdot R_v}{R_d + R_f + R_v} \cdot q_b - \frac{R_v \cdot (R_d + R_f)}{R_d + R_f + R_v} \cdot q_{uf} + \frac{R_d + R_f}{R_d + R_f + R_v} \cdot P_v.$$

These equations can be rewritten as reported herein below.

$$P_{af} = c_{a0} \cdot P_a + c_{a1} \cdot q_b + c_{a2} \cdot q_{uf} + (1 - c_{a0}) \cdot P_v$$

$$P_{vf} = c_{v0} \cdot P_a + c_{v1} \cdot q_b + c_{v2} \cdot q_{uf} + (1 - c_{v0}) \cdot P_v$$

5   in which:

$$c_{a0} = \frac{R_f + R_v}{R_d + R_f + R_v} \qquad c_{a1} = -\frac{R_d \cdot R_f}{R_d + R_f + R_v} \qquad c_{a2} = -\frac{R_d \cdot R_v}{R_d + R_f + R_v}$$

$$c_{v0} = \frac{R_v}{R_d + R_f + R_v} \qquad c_{v1} = \frac{R_f \cdot R_v}{R_d + R_f + R_v} \qquad c_{v2} = -\frac{R_v \cdot (R_d + R_f)}{R_d + R_f + R_v}$$

The third operating mode (as the following fourth and fifth operating modes) calculates at least a part of the coefficients

10   c_{a0}, c_{a1}, c_{a2} and c_{v0}, c_{v1}, c_{v2} and from these derives R_d, R_f and R_v. The calculation of the coefficients is done starting from one or more known values for each of the following quantities: P_a, q_b, q_{uf}, P_v, P_{af} and P_{vf}. The quantities P_a, q_b, q_{uf}, P_v are known through measurement. The quantities P_{af} and P_{vf} are known by

15   direct measurement of the pressures in the vascular access, or by a process of calculation starting from the measurement of the pressures in the machine P_{am} and P_{vm}.

As the number of coefficients c_{a0}, c_{a1}, c_{a2}, c_{v0}, c_{v1}, c_{v2} is greater than the number of the resistances R_d, R_f and R_v, there exists a

20   multiplicity of relations between the coefficients and the resistances. In general, knowledge of three coefficients enables a determination of the resistances.

In the third operating mode both flow rates q_b and q_{uf} are varied and the arterial pressure in the machine P_{am} is measured, from

25   which arterial pressure in the vascular access P_{af} is calculated.

In a specific embodiment in a first stage the pressure P_{am} at

flow rates $q_b = 0$ and $q_{uf} = 0$ is measured; in a second stage pressure P_{am} at flow rates $q_b \neq 0$ and $q_{uf} = 0$ is measured; in a third stage pressure P_{am} at flow rates $q_b \neq 0$ and $q_{uf} \neq 0$ is measured.

5   More in general, q_b at $q_{uf} = $ constant (for example = 0) is varied and P_{am} is measured at different values of q_b. Thereafter q_{uf} at $q_b = $ constant (for example $\neq 0$) is varied and P_{am} measured at different values of q_{uf}.

In this third operating mode a mathematical model of the
10   vascular access is used which is represented by one equation only:

$$P_{af} = c_{a0} \cdot P_a + c_{a1} \cdot q_b + c_{a2} \cdot q_{uf} + (1 - c_{a0}) \cdot P_v$$

from which coefficients c_{a0}, c_{a1}, c_{a2} can be derived, which are sufficient by themselves for the calculation of the three
15   resistances R_d, R_f, R_v.

In this third operating mode at least one measurement is taken of the patient's arterial pressure P_a. Further, distal venous pressure P_v is assumed to be zero; for this reason the equation used is simplified as follows:

20    $$P_{af} = c_{a0} \cdot P_a + c_{a1} \cdot q_b + c_{a2} \cdot q_{uf}$$

The third operating mode is now described step by step.

a.   Determine values P_{af0} of the arterial pressure in the vascular access (fistula) and the systemic arterial pressure of the patient P_{a0} at a known ultrafiltration flow
25   rate $q_{uf1} = 0$ at a predetermined blood pump flow rate $q_b = 0$.

b.   Save and store values P_{a0} and P_{af0}.

c.   Calculate c_{a0} by means of the equation

$$c_{a0} = \frac{P_{af0}}{P_{a0}}$$

d. Save and store value c_{a0}.

e. Change the blood flow rate q_b to a known value q_{b1}. At the same time the ultrafiltration flow rate q_{uf} is kept constant and equal to the flow rate at point a. (= 0).

5   f. Determine values P_{af1} and P_{a1} of the arterial pressure in the vascular access (fistula) and, respectively, of the patient at blood pump flow rate q_{b1}.

g. Save and store values q_{b1}, P_{af1} and P_{a1}.

h. Steps d-f can be repeated for a desired number of times so
10   as to save and store a series of values q_{bi}, P_{afi}, P_{ai}, with i = 1, 2, 3, …, N, where N is an integer number greater than or equal to 1.

i. Determine c_{a1} by solving the system of equations:

$$P_{afi} - c_{a0} \cdot P_{ai} = c_{a1} \cdot q_{bi}$$

15   with i = 1, …, N (N ≥ 1)

If N = 1 it is sufficient to solve a linear equation with only an unknown quantity.

If N > 1 the value of c_{a1} is found by means of an optimisation algorithm which determines the optimal
20   solution for the above-cited system. The searched-for value can be the value of c_{a1} which minimises the error between the values of P_{af} calculated with the above system of equations, $P_{afi}*$, where the asterisk * indicates that the value has been calculated, and the P_{afi} values determined by
25   measuring a pressure correlated with P_{af}. The optimisation algorithm can be, for example, a linear regression algorithm.

j. Save and store value c_{a1}.

k. Change the ultrafiltration flow rate to a known value q_{uf1}

not zero. At the same time the blood flow rate q_b has a known value q_{bk} different to zero.

l. Determine values P_{af1} and P_{a1} of the arterial pressure in the vascular access (fistula) and, respectively, of the patient at ultrafiltration flow rate q_{uf1}.

m. Save and store values q_{bk}, q_{uf1}, P_{af1} and P_{a1}.

n. Steps k-m can be repeated for a desired number of times in order to store a series of values q_{ufj}, P_{afj}, P_{aj}, with $j = 1$, 2, …, M, where M is an integer number equal to or greater than 1.

o. Determine c_{a2} by solving the following system of equations

$$P_{afj} - c_{a0} \cdot P_{aj} - c_{a1} \cdot q_{bk} = c_{a2} \cdot q_{ufj}$$

with $j = 1, 2, …, M$ $(M \geq 1)$

If $M = 1$ it is sufficient to solve a linear equation with only an unknown quantity.

If $M > 1$ the value of c_{a2} is found by means of an algorithm of optimisation which determines the optimal solution for the above system. The sought-after value can be the value of c_{a2} which minimises the error between the values of P_{af} calculated using the system of equations $P_{afj}*$, where the asterisk * indicates that the value is a calculated one, and the values of P_{afj} determined through measuring a pressure correlated by P_{af}. The optimisation algorithm can be, for example, a linear regression algorithm (as at point i. above).

p. Save and store the determined value of c_{a2}.

q. Determine R_f, R_v and R_d by solving the following system of equations which express the relation between c_{a0}, c_{a1}, c_{a2} and R_d, R_f, R_v.

$$R_f = -c_{a1} \cdot \left(1 + \frac{1}{1/c_{a0} - 1}\right)$$

$$R_v = -c_{a2} \cdot \left(1 + \frac{1}{1/c_{a0} - 1}\right)$$

$$R_d = \left(1/c_{a0} - 1\right) \cdot \left(R_f + R_v\right)$$

The value of the resistance R_f can already be determined at step j. as both c_{a0} and c_{a1} are already known.

r.   Save and store the first determined values of R_f, R_v and R_d.

s.   Determine q_a using one of the equations of the mathematical model of the vascular access, for example:

$$q_a = \frac{P_a - P_{af}}{R_d}$$

t.   Save and store the value calculated for q_a.

In steps from 1. to n. the operation of measuring P_{aj} can be omitted; in this case the values stored and used for the calculation are the same P_{ai} values calculated at point h. at $q_b = q_{b1}$ and $q_{uf} = 0$, or at point a. at $q_b = 0$ and $q_{uf} = 0$.

Fourth monitoring procedure.

Varying q_b at q_{uf} = constant (for example zero) and measuring P_{am} and P_{vm}.

In this case too we calculate at least a part of the coefficients c_{a0}, c_{a1}, c_{a2} and c_{v0}, c_{v1}, c_{v2} from which R_d, R_f and R_v are obtained. The calculation of the coefficients is done starting from the knowledge of one or more values for each of the following quantities: P_a, q_b, q_{uf}, P_v, P_{af} and P_{vf}. The quantities P_a, q_b, q_{uf}, P_v are known by measurements. The quantities P_{af} and P_{vf} are known by direct measurement of the pressures in the vascular access, or by means of a calculation process which uses the measured values of pressures P_{am} and P_{vm}

in the extracorporeal circuit.

In the fourth operating mode the measures were taken at $q_{uf} = 0$ and we use a mathematical model which includes both equations of P_{af} and P_{vf} which in this case are simplified into the following

5   formulation:

$$P_{af} = c_{a0} \cdot P_a + c_{a1} \cdot q_b + (1 - c_{a0}) \cdot P_v$$

$$P_{vf} = c_{v0} \cdot P_a + c_{v1} \cdot q_b + (1 - c_{v0}) \cdot P_v$$

In the fourth operating mode the processor determines the four coefficients c_{a0}, c_{a1}, c_{v0}, and c_{v1} and from these it calculates

10   the three resistances R_d, R_v, R_f.

In the fourth operating mode the pressures P_{af} and P_{vf} in the vascular access are determined, either by direct measuring or by measuring pressures P_{am} e P_{vm} in the extracorporeal circuit and calculating P_{af} and P_{vf} by means of a mathematical model. The

15   pressures P_{af} and P_{vf} are determined at different values of the blood flow rate q_b. In the fourth operating mode, the arterial and venous pressures P_a and P_v of the patient are also considered in the calculation of the coefficients.

As coefficients c_{a0}, c_{a1}, c_{v0}, and c_{v1} are greater in number than

20   resistances R_d, R_f and R_v, there exists a multiplicity of relations between the coefficients and resistances. In general the knowledge of three coefficients enables determination of the resistances. It has been found that the most precise determination of the resistances R_d, R_f and R_v is obtained by

25   using the three coefficients, c_{a0}, c_{a1}, and c_{v0}.

The fourth operating mode is now described step by step.

a.   Determine pressures P_{af}, P_{vf}, P_a, and P_v with the blood pump flow rate and the ultrafiltration flow rate at nil ($q_b = 0$ and $q_{uf} = 0$).

30   b.   The values thus determined, P_{af0}, P_{vf0}, P_{a0} and P_{v0}, are stored

in memory.

c. The processor calculates c_{a0} and c_{v0} by means of the equations:

$$c_{a0} = \frac{P_{af0} - P_{v0}}{P_{a0} - P_{v0}}$$

$$c_{v0} = \frac{P_{vf0} - P_{v0}}{P_{a0} - P_{v0}}$$

d. Change the blood flow rate to a known value $q_b = q_{b1} \neq 0$.

e. Determine at least one value of P_{af}, P_{vf}, P_a and P_v when $q_b = q_{b1}$.

f. Save and store values P_{af1}, P_{vf1}, P_{a1} and P_{v1} above-determined.

g. Repeat steps from d. to f. for a predetermined number of times N in order to obtain a series of values q_{bi}, P_{afi}, P_{vfi}, P_{ai} and P_{vi} with i = 1, 2,…, N (N ≥ 1).

h. Calculate c_{a1} as a solution for the system of equations

$$P_{afi} - c_{a0} \cdot P_{ai} - (1 - c_{a0}) \cdot P_{vi} = c_{a1} \cdot q_{bi}$$

If N = 1 the solution is immediate. If N > 1 the solution is obtainable with an optimization algorithm, such as for example a linear regression algorithm.

i. Save and store the value of c_{a1}.

j. Determine resistances R_d, R_f, and R_v by solving the following equations which express the relation between c_{a0}, c_{a1}, c_{v0} and R_d, R_f, R_v:

$$R_d = \frac{c_{a1}}{c_{v0} - c_{a0}}$$

$$R_f = \frac{c_{a1}}{c_{a0} - 1}$$

$$R_v = \frac{c_{a1} \cdot c_{v0}}{(c_{a0} - c_{v0}) \cdot (c_{a0} - 1)}$$

k. Save and store values R_d, R_f, and R_v above-determined.

l. Determine the flow rate of the vascular access q_a using one of the equations of the mathematical model, for example the second:

$$P_{af} - P_{vf} = R_f \cdot (q_a - q_b)$$

At point e., determination of the value of P_v can be performed in two ways.

The first consists in considering P_v constant ($P_v = P_{v0}$) during variation in the blood flow rate q_b, thus ignoring the variations in the venous pressure P_v which actually occur during the various operative stages. Consequently the system of equations of point h. can be rewritten in the following way:

$$P_{afi} - c_{a0} \cdot P_{ai} - (1 - c_{a0}) \cdot P_{v0} = c_{a1} \cdot q_{bi}$$

The second way consists in considering the variations in P_v to be proportional to the variations in the arterial pressure P_a, thus:

$$P_{vi} = P_{v0} \cdot \frac{P_{ai}}{P_{a0}}$$

This is equivalent to assuming resistances R_d, R_f and R_v to be constant during variation of q_b.

In this case the equation of point h. is:

$$P_{afi} - c_{a0} \cdot P_{ai} - (1 - c_{a0}) \cdot P_{v0} \cdot \frac{P_{ai}}{P_{a0}} = c_{a1} \cdot q_{bi}$$

Note that by substituting, in the above equation, c_{a0} with the expression

$$c_{a0} = \frac{P_{af0} - P_{v0}}{P_{a0} - P_{v0}}$$

as in point c. of the present operating mode, the following equation is obtained:

$$P_{afi} - \frac{P_{af0}}{P_{a0}} \cdot P_{ai} = c_{a1} \cdot q_{bi}$$

5   which is the same equation that appears at point i. of the third operating mode, in which the contribution of P_v was ignored.

Fifth monitoring procedure.

The fifth operating mode is similar to the third, with the difference that, instead of determining P_{af}, P_{vf} is determined.

10   Briefly, the fifth operating mode consists in varying the blood flow rate q_b while maintaining the ultrafiltration rate q_{uf} constant, in varying the ultrafiltration rate while keeping the blood flow rate q_b constant, and in determining the venous pressure in the vascular access P_{vf} at various values of the

15   above-mentioned flow rates. The processor determines the resistances R_d, R_f and R_v and the flow rate q_a in the vascular access by calculating the coefficients c_{v0}, c_{v1}, c_{v2} using the equation

$$P_{vf} = c_{v0} \cdot P_a + c_{v1} \cdot q_b + c_{v2} \cdot q_{uf} + (1 - c_{v0}) \cdot P_v$$

20   and the operative stages cited for the third operative mode.

The resistances are calculated by solving the following system of equations:

$$c_{v0} = \frac{R_v}{R_d + R_f + R_v}$$

$$c_{v1} = \frac{R_f \cdot R_v}{R_d + R_f + R_v}$$

$$c_{v2} = -\frac{R_v \cdot (R_d + R_f)}{R_d + R_f + R_v}$$

The flow rate of the vascular access q_a is calculated as in the third operative mode.

Note that, by means of the second monitoring procedure, q_a and R_v can be derived by determining two or more values for the venous pressure alone (P_{vm} in the machine or P_{vf} in the fistula), with the equation

$$P_{vf} - P_v = R_v \cdot (q_a - q_{uf})$$

while for the calculation of the values of R_f and R_d, the values of arterial pressure (P_{am} or P_{af}) are also used, as well as the other two equations of the mathematical model:

$$q_a = \frac{P_a - P_{af}}{R_d} \quad \text{and} \quad P_{af} - P_{vf} = R_f \cdot (q_a - q_b).$$

Similarly a further monitoring procedure can be formulated on the basis of which the values of q_a and R_d are calculated, determining two or more values of only the arterial pressure (P_{am} in the machine or P_{af} in the fistula), using the equation

$$q_a = \frac{P_a - P_{af}}{R_d}$$

while for calculating the values of R_f and R_v the values of the venous pressure (P_{vm} or P_{vf}) are also used, as well as the other two equations of the mathematical model:

$$P_{vf} - P_v = R_v \cdot (q_a - q_{uf}) \quad \text{and} \quad P_{af} - P_{vf} = R_f \cdot (q_a - q_b).$$

In all of the above-described modes, the measurements are taken with the system in a steady state. For example, the various measurements are taken after a certain time interval (for example about ten seconds) after the blood flow rate or the ultrafiltration rate has been changed.

Two numerical examples of the application of the invention are now reported.

First example.

This example uses the above-described first monitoring procedure, applied to the apparatus of figure 1.

Direct measurement of pressures P_a, P_{af}, P_{vf} were taken at different flow rate values q_b. The measurements taken are reported in the following table.

q_b	P_a	P_{af}	P_{vf}	ΔP_f
(ml/min)	(mmHg)	(mmHg)	(mmHg)	(mmHg)
300	100	51	42	9
200		52	41	11
100		54	40	14
400		51	42	9
500		50	43	7

The equation of the straight line interpolating points ΔP_f is as follows (see figure 4, where ΔP_f is a function of q_b):

$\Delta P_f = 0.016 \cdot (925 - q_b)$

From which the following values are calculated

$R_f = 0.016$ mmHg min/ml

$q_a = 925$ ml/min

From the third equation of the mathematical model used (assuming $P_v = 0$) we have $q_{b1} = 300$ ml/min:

$$R_v = \frac{P_{vf1}}{q_a} = 0.045 \text{ mmHg} \cdot \text{min/ml}$$

Given P_a = 100 mmHg, for q_{b1} = 300 ml/min we obtain:

$$R_d = \frac{P_a - P_{af1}}{q_a} = 0.053 \text{ mmHg}\cdot\text{min/ml}$$

Second example.

The second example uses the fourth monitoring procedure.

5 In the following the values of the pressure measured at different blood pump flow rates are reported.

q_b	P_a	P_{af}	P_{vf}	P_v
(ml/min)	(mmHg)	(mmHg)	(mmHg)	(mmHg)
0	120	62	35	0
150	118	59	37	
250	117	57	37	
350	114	53	38	

From these values we obtain:

$$c_{a0} = \frac{P_{af0} - P_{v0}}{P_{a0} - P_{v0}} = 0.52$$

$$c_{v0} = \frac{P_{vf0} - P_{v0}}{P_{a0} - P_{v0}} = 0.29$$

10 By applying a linear regression algorithm to the following equation:

$$P_{afi} - c_{a0} \cdot P_{ai} - (1 - c_{a0}) \cdot P_{v0} = c_{a1} \cdot q_{bi}$$

the following value for coefficient c_{a1} was found:

c_{a1} = -0.0155

15 After which the following resistance values were found:

R_d = 0.069 mmHg min/ml

R_f = 0.032 mmHg min/ml

R_v = 0.042 mmHg·min/ml

From this we calculated:

5 $$q_a = \frac{P_{af0} - P_{vf0}}{R_f} = 842 \text{ ml/min}$$